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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KIM, YUNSOO	

ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/579,357	BOLLI ET AL.	
	Examiner	Art Unit	
	YUNSOO KIM	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 February 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-13,15,16,18,21,24,25 and 27-44* is/are pending in the application.

4a) Of the above claim(s) *18,20,21,24,25 and 27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-13,15,16,23 and 28-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/16/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1, 4-13, 15, 16, 18, 20, 21, 24-25 and 27-44 are pending.

Claims 18, 20, 21, 24, 25 and 27 stand withdrawn from further consideration by the examiner under 37 CFR 1.142 (b) as being drawn to a nonelected invention.

Claims 1, 4-13, 15, 16 and 28-44 are currently being examined in the instant application.

2. Applicants' IDS filed on 2/16/10 has been acknowledged.

3. In light of Applicant's amendments filed on 2/16/10, the following rejections remain (note sections 12-13 set forth in the office action mailed on 11/16/09 have been withdrawn).

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> /b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claim 8 stands rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Pat. No. 5,831,736 (IDS reference, of record) for the reasons set forth in the office action mailed on 11/16/09.

The '736 patent teaches IgG formulation for intravenous administration at 3-16% w/v (preferably 6-12% w/v) concentration of IgG and a naturally occurring amino acid proline at least 200mM at pH range 5-6 and at 5.3 (col. 2-3, overlapping paragraph, col. 4, lines 55-60, Example 1, claims 1-14).

Given that the claimed invention does not exclude addition of nicotinamide as recited in claim 1 of the instant application and claim 8 recites "comprising" which is considered open, addition of nicotinamide does not exclude the '736 patent from prior art. Therefore, the reference teachings anticipate the claimed invention.

Applicant's arguments filed on 2/16/10 have been fully considered but they were not persuasive.

Applicant has asserted that the dependency of claims 9-13 have been changed to the independent claim 1 instead of 8 and the rejection is moot.

In light of Applicant's amendments, the rejection based on claims 1—11, 15, 16 and 28-40 have been withdrawn.

However, claim 8 does not exclude nicotinamide and uses "comprising", the '736 patent is a proper anticipatory reference and the rejection is maintained.

6. Claims 1, 4-8, 10-13, 15, 16, 23 and 28 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Pub. 2005/0142139A1, of record, as is evidenced by the specification of the instant application on p. 4 and 6 for the reasons set forth in the office action mailed on 11/16/09.

Applicant's arguments filed on 2/16/10 have been fully considered but they were not persuasive.

Note the rejection of claims 29-40 has been withdrawn as the current claim amendment in claims 29, 35, 37 and 38 recite "polyclonal".

Applicant has asserted that the rejection in that the '139 publication is for CD4-IgG2 chimeric tetramer but the claimed formulation comprises IgG which has different structure from the CD4-IgG2 chimeric tetramer. Applicant has further asserted that the '139 publication is not a proper anticipatory reference as it fails to teach all the limitations of the claimed invention. Applicant has further asserted that the specification of the instant application defines the immunoglobulin may be of any idiotype but preferably IgG, IgA or IgM and the fused prior art protein is not an immunoglobulin.

Contrary to Applicant's arguments, the claimed composition of claim 1 does not recite IgG but any immunoglobulin. Moreover, the '139 publication teaches that CD4-IgG2 construct with CD4 regions grafted in variable regions of IgG2. Note that all IgG is a tetramer comprising 2 heavy chains and 2 light chains. Therefore, Applicant's assertion that the '139 publication fails to teach all the limitations of the claimed invention based on the non-claimed IgG and IgG structures of the '139 publication is misleading. Therefore, the '139 publication is a proper anticipatory reference and the rejection is maintained.

Further, the specification of the instant application discloses (p.5, lines 14-25) that the immunoglobulin is obtained from blood plasma, recombinant DNA technology, and combined with any purification techniques. Moreover, the specification clearly indicates that the immunoglobulins are subject to enzymatic digestion and the whole immunoglobulins can be used (contemplating that the fragments of immunoglobulin can be also used). Note that the prior art CD4-IgG2 is generated by enzymatic digestion of IgG2 and the fusion of CD4 (p. 3-4). As Applicant has acknowledged that the immunoglobulin is a protein (p.5) and the chimeric antibody is not excluded from the immunoglobulin, therefore, the prior art antibody reads on the claimed immunoglobulin.

As discussed previously, the '139 publication teaches CD4-IgG2 antibody formulation comprising a histidine buffer and proline at about pH 5.5 (claims 29-39, [0032]). Given that the specification on p.4 of the instant application discloses that all naturally occurring amino acid is L-amino acid and the '139 publication discloses naturally occurring amino acids, claim 4 is included in this rejection.

As the '139 publication does not disclose any use of nicotinamide as a stabilizer, the referenced formulation is considered to be made in the absence of nicotinamide. Thus, meets the claimed limitation of claim 1.

Further, the '139 publication teaches that the concentration of the antibody is 15-162mg/ml ([0045-47]) and proline concentration of "about" 25-150mM ([0013]).

Note the term "about" is flexible and includes unrecited limitations near the recited limitation. Given that the '139 publication teaches the proline concentration of "about"150mM and reads on claimed limitation of "at least 0.2M" or "0.2M", claims 7 and 8 are included in this rejection.

As is evidenced by the specification on p. 6 of the instant application, 10% of IgG is equivalent to 100g/L. Given that the concentration of 100g/L is equivalent to 100mg/ml, the referenced about 100-162mg/ml that are suitable for subcutaneous or IV are equivalent to 10-16.2% (w/v) ([0007, 0049]) and claims 10-13 are included in this rejection.

Moreover, the referenced histidine buffer is considered as "pharmaceutically acceptable additives", claims 16 and 23 are included in this rejection. Further, claims 34, 36 and 40 reciting "wherein the preparation is a liquid preparation that has not been subject to lyophilization" are included in this rejection because the '139 publication specifically recites "stable following at least one freeze and thawing of formulation" (claim 16) which differentiate the physical condition of the formulation from recited "lyophilized"(claim

15) which is subject to lyophilization. Therefore, the reference teachings anticipate the claimed invention.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1, 7-9 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Pub. 2005/0142139A1, of record, for the reasons set forth in the office action mailed 11/16/09.

The '139 publication has been discussed, supra.

The referenced concentration range of proline is about 25-150mM ([0032-34]). Note the term "about" is flexible and includes unrecited limitations near the recited limitation. Given that the '139 publication teaches the proline concentration of "about"150mM and reads on claimed limitation of "at least 0.2M", "0.25M", "0.2 to 0.3M" or "0.2 to 0.4M" of proline as recited claims 7-9 and 28 of the instant application.

As the general conditions of the claims are disclosed in the reference, it is not inventive to discover the optimum or workable ranges by routine examination. Further, a prima facie case of obviousness exists where the claimed ranges and prior ranges do not overlap but are close enough that one skilled in the art would have expected to have the same property.

Note the referenced "about 150mM of proline" is considered close enough to the claimed "at least 0.2M", "0.25M" or " 0.2 to 0.4M" of proline as in claims 7-9 and 28 of the instant application. See MPEP 2144.05. Therefore, the claimed preparation is included in the formulation taught by the reference in the absence of showing any unobvious differences.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by reference, especially in the absence to the contrary.

Applicant's arguments filed on 2/16/10 have been fully considered but they were not persuasive.

Note the rejection of claims 29-40 has been withdrawn as the current claim amendment in claims 29, 35, 37 and 38 recite "polyclonal".

Applicant has asserted that the '139 publication is not a proper anticipatory reference and does not provide a basis for obviousness rejection.

In light of discussion above in sections 4 and 6 of this office action, the obviousness rejection has been maintained.

9. The following new ground of rejection is necessitated by Applicant's amendments filed on 2/16/10.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1, 4-13, 15, 16 and 28-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Pat. No. 6,171,586 (IDS reference filed on 5/16/06) in view of U.S. Pub. 2005/0142139A1(of record).

The '586 patent teaches a stable aqueous pharmaceutical formulation comprising a buffer at about pH 4.8 and the antibody encompasses polyclonal antibody (col. 7-8, claims 1-29).

Given that the '586 patent does not disclose nicotinamide, the claimed limitation "wherein the preparation does not comprise nicotinamide" has been met.

The disclosure of the '586 patent differs from the claimed invention in that it does not teach the use of proline as is currently recited in claim 1 of the instant application.

The '139 publication has been discussed, supra.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to add proline as a stabilizer as taught by the '139 publication to the antibody formulation as taught by the '586 patent.

Therefore, it is prima facie obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose; idea of combining them flows logically from their having been individually taught in prior art. In re Kerkhoven, 205 USPQ 1069, CCPA 1980. See MPEP 2144.06

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the addition of proline improves stability of protein upon storage and delivery by reducing aggregation.

From the teachings of the references, it would have been obvious to one of ordinary skill in the art to combine teachings of the references and there would have been a reasonable expectation to success in producing the claimed invention. Therefore, the invention as a whole was a prima facie obvious to one of ordinary skill in the art at the time the invention was made as evidenced by the references, especially in the absence of evidence to the contrary.

12. No claims are allowable.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to YUNSOO KIM whose telephone number is (571)272-3176. The examiner can normally be reached on M-F, 9-5. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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May 11, 2010

/Michael Szperka/
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